## AMENDMENTS TO THE DRAWINGS

Please replace informal Figure 1 with attached formal Figure 1.

## REMARKS

Claim 14 has been amended. Claims 2-7, 9, and 12-15 remain pending in the present application. Support for the amendments is found in the specification and claims as filed. Accordingly, the amendments do not constitute the addition of new matter. Reconsideration of the application in view of the foregoing amendments and following comments is respectfully requested.

Objection to Drawings

Figure 1 was objected to for being a color photograph without a petition. Informal Figure 1 has now been replaced with formal Figure 1, which is a black and white photograph of the same matter. Accordingly, no new matter has been added. Applicants respectfully request the Examiner to reconsider and withdraw the objection to the figure.

Rejection of Claims under 35 U.S.C. § 112

The Examiner rejected Claims 14 and 15 under 35 U.S.C. § 112, second paragraph, for being vague and indefinite because Claims 14 and 15 are dependent on cancelled Claim 10. Claim 14 has been amended to depend on Claim 2 or 9.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 112, second paragraph.

Rejection of Claims under 35 U.S.C. § 103

The Examiner rejected Claims 2, 5-7, 9, and 14-15 under 35 U.S.C. § 103(a) as being unpatentable over Bianchi et al. (*Prenatal Diagnosis*, Vol. 13, 293-300, 1993) in view of Hume et al. (*Early Human Development*, Vol. 42, No. 2, 1995, pp. 85-95) and Hume et al. (*Blood* , Vol. 87, No. 2, 1996, pp. 762-770).

Claim 2 recites "[a] method of isolating embryonic or fetal red blood cells from a sample containing maternal blood cells and embryonic or fetal blood cells or both, the method comprising determining which cell or cells contain or express an adult liver component that is a cell surface exposed component, wherein the adult liver component is not transferrin receptor,

the method comprising the steps of: (a) contacting the sample with a binding moiety that specifically binds the adult liver component; (b) allowing the binding moiety to bind to the adult liver component; and (c) isolating the embryonic or fetal red blood cells by virtue of being bound to the binding moiety."

Claim 9 recites "A method of isolating embryonic or fetal red blood cells from a sample containing maternal blood cells and embryonic or fetal blood cells or both, the method comprising isolating the cells which contain or express a component selected from the group consisting of glucose transporter 2 (GLUT2), a P-glycoprotein, a multi-drug resistance protein (MDRP), a multi-drug resistance-like protein (MRP), γ-glutamyl transpeptidase, a lipoprotein receptor, an alkaline phosphatase, a bile salt transporter, a hormone receptor, a multiple organic ion transporter (MOAT), a bilirubin transporter, and a bilirubin conjugate transporter, the method comprising the steps of: (a) contacting the sample with a binding moiety that specifically binds the component; (b) allowing the binding moiety to bind to the adult liver component; and (c) isolating the embryonic or fetal red blood cells by virtue of being bound to the binding moiety."

Bianchi et al. teaches a method of isolating fetal nucleated cells from maternal blood. The Examiner admits that Bianchi et al. does not teach a method of identifying and isolating embryonic or fetal red blood cells via an adult liver component that is cell surface exposed. However, the Examiner cites Hume et al. (*Early Human Development* ref.) and Hume et al. (*Blood* ref.) to disclose the use of antibodies to glucose-6-phosphatase which is an adult liver component.

Bianchi et al. compared the effectiveness of three monoclonal antibodies for the separation of fetal cells from maternal blood by flow sorting. In Bianchi et al., the blood cells of pregnant women were incubated with antibodies that recognized surface antigens. Accordingly, the separation of cells in Bianchi relies on recognizing cell surface antigens. In the previous Amendment, it was argued that the proteins in the Hume et al. references are not cell surface exposed components. Nevertheless, the Examiner's position is that glucose-6-phosphatase "exits [sic?] in either state (cell surface exposed or intracellular component) absent evidence to the contrary."

However, indeed, glucose-6-phosphatase is not exposed on the cell surface of fetal cells. Glucose-6-phosphatase has been known and used as an endoplasmic reticulum marker since the 1950's and is clearly intracellular. This endoplasmic reticulum localization of glucose-6-phosphatase is acknowledged in both of the Hume et al. references. Hume et al. (1995) recites on page 86, second paragraph: "Glucose-6-phosphatase is located in the endoplasmic reticulum..." Hume et al. (1996) recites in the abstract, lines 1-5 and page 762, left column, lines 12-13: "The catalytic subunit of the glucose-6-phosphatase enzyme is situated with its active site inside the lumen of the endoplasmic reticulum."

Accordingly, the accepted scientific viewpoint is that glucose-6-phosphatase is an intracellular component. The prior art, as argued above as showing that glucose-6-phosphatase is an intracellular component, has not demonstrated "[a] method of isolating embryonic or fetal red blood cells from a sample containing maternal blood cells and embryonic or fetal blood cells or both, the method comprising determining which cell or cells contain or express an adult liver component that is a cell surface exposed component," as recited in Claim 2. Also, glucose-6-phosphatase is not recited as one of the components in the Markush group of Claim 9. Accordingly, the pending claims are nonobvious over the recited prior art.

The Examiner rejected Claim 13 under 35 U.S.C. § 103(a) as being unpatentable over Bianchi et al. (*Prenatal Diagnosis*, Vol. 13, 293-300, 1993) in view of Hume et al. (*Early Human Development*, Vol. 42, No. 2, 1995, pp. 85-95) and Hume et al. (*Blood* , Vol. 87, No. 2, 1996, pp. 762-770) and in further view of Maggio (*Immunoenzyme Technique I*, CRC Press, 1980, pp. 186-187).

According to M.P.E.P. 2143.03, "[i]f an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious." Claim 13 is dependent on Claim 2. As argued above, Claim 2 is nonobvious over the prior art. Accordingly, Claim 13 is also nonobvious over the prior art.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing amendments and comments, it is respectfully submitted that the present application is fully in condition for allowance, and such action is earnestly solicited.

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless , if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully requested to call the undersigned in order to resolve such issue promptly.

Respectfully submitted,

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